AACC/NKF Guidance Document on Improving Equity in Chronic Kidney Disease Care

Article:
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Guests: Dr. Christina Pierre from the Department of Pathology and Laboratory Medicine at the Perelman School of Medicine at the University of Pennsylvania and Dr. Joseph Vassalotti from the National Kidney Foundation and the Division of Nephrology at the Icahn School of Medicine at Mount Sinai.

Randye Kaye: Hello and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Until recently, the use of Black race coefficients in estimated glomerular filtration rate, or eGFR, equations reported from serum creatinine tests was standard practice in most clinical laboratories. However, in September of 2021, the National Kidney Foundation and the American Society of Nephrology Task Force on Reassessing the Inclusion of Race in Diagnosing Kidney Diseases released a report which outlined a new race-free approach to diagnosing kidney disease. The NKF-ASN Task Force recommendations included the adoption of a new eGFR 2021 CKD-EPI creatinine equation that estimates kidney function without a race variable. The task force also recommended increased use of cystatin C combined with creatinine as a confirmatory assessment of GFR or kidney function.

The July 2023 issue of *JALM* features the AACC Academy's most recent guidance document, the "AACC/NKF Guidance Document on Improving Equity in Chronic Kidney Disease Care," which was a collaboration with the National Kidney Foundation. Intended as a tool for implementation of the NKF-ASN Task Force recommendations, the document provides a framework for understanding the nuances and potential harms of utilizing race as a biological classifier in eGFR. The document provides evidence-based actionable measures for clinical laboratories to improve equity in kidney health. Further, because the new eGFR equations continue to use the patient's sex as variable, the document provides considerations for reporting eGFR in transgender and gender-diverse individuals.

Today we are joined by two authors from the guidance document. Dr. Christina Pierre is a board-certified clinical

chemist and a Clinical Assistant Professor in the Department of Pathology and Laboratory Medicine at the Perelman School of Medicine at the University of Pennsylvania. Dr. Pierre co-chaired the guidance document with Dr. Dina Greene. With Dr. Pierre today, we also have Dr. Joseph Vassalotti. Dr. Vassalotti is the Chief Medical Officer of the National Kidney Foundation and is a Clinical Professor of Medicine in the Division of Nephrology at the Icahn School of Medicine at Mount Sinai. Welcome Drs. Pierre and Vassalotti. Firstly, can you provide us with more context about why the new CKD-EPI equations were developed?

Christina Pierre: Yeah. So, race was initially included in eGFR equations by the researchers that were developing them based on observations of higher creatinine in Black versus non-Black people. But we know now that the use of race in science and medicine has been -- it is increasingly being challenged, I should say. We know that race is very nebulously defined. It is a social system of classification. It really doesn't describe, or accurately describe rather, the biological variation between humans, and I think another really important point to make is that race, as we understand it today, was really developed and born out of oppression. So based on these premises, the NKF and the American Society for Nephrology re-evaluated the use of race in eGFR equations and unanimously decided that we should use a race-agnostic approach.

Joseph Vassalotti: I think I would agree with everything you said. I think it's great that the National Kidney Foundation and the AACC are working together here on this document. I would just add that when we include race in calculations, we risk really validating disparities rather than recognizing as something that we need to improve or eliminate completely in medicine.

Randye Kaye: Why is it important for clinical laboratories to implement these new equations?

Christina Pierre: Well first of all, as I mentioned before, the social cost of inclusion of race is really just too high. Also, we now know that we can compute eGFR estimates that perform satisfactorily clinically without using race and without incorporating race. I also think it's important to touch on the combined equation that utilizes cystatin C. So, cystatin C testing isn't as widely used in clinical laboratories, but we know that the combined CKD-EPI 2021 equation that uses both creatinine and cystatin C offers more accurate estimates, so implementation of that equation is also really important.

And then lastly, I just wanted to touch on standardization. So, there's poor standardization across laboratories in terms of which eGFR equation is used, as well as for kidney disease biomarker reporting, and harmonization of the equation that

we use to estimate GFR really assist clinicians to detect and manage kidney disease better.

Randye Kaye: All right, wonderful. I have a personal stake in this since I have a brother with kidney disease right now and so I'd like to know what are some risk factors for chronic kidney disease? What groups are at increased risk?

Joseph Vassalotti: Well, there's a very long list of risk factors, but the guidance document really focuses on four of them: diabetes, hypertension, cardiovascular disease, and a family history of kidney failure. The family history of CKD or kidney disease isn't included because we don't really have as much data on that as we do for kidney failure. I think it's important that we recognize that there are genetic risks as well, although these are less important than some of the other risk conditions, but genetic ancestry and APOL1 is reviewed in the paper. Apolipoprotein L1 that's common in individuals of West African ancestry that does carry an increased risk for chronic kidney disease. And then I think I would be remiss if I didn't mention disparities and that we're increasingly recognizing that the social risk factors that we used to focus on in the past, race and ethnicity, really translate to social determinants of health.

Social Deprivation Index is a major risk factor for kidney disease, that's reviewed in the guidance document, and also unfortunately racism and systemic issues in our society and in medicine contribute some of the disparities in kidney health, which include not only poor blood pressure and diabetes control, but also poor access to nephrology care and poor access to kidney replacement therapy options like kidney transplant and home dialysis.

Randye Kaye: All right, thank you so much. So with the implementation of the new CKD-EPI equations, what changes or impacts can we expect to see?

Joseph Vassalotti: Well I think for one, it's important that clinicians and patients pay attention to estimated GFR. It's important that clinicians and patients are clear which equation is being reported and if they're not clear, they can work with their clinical laboratory to find out, to ensure that the recommended CKD-EPI 2021 equation is being reported and of course, a simple way of knowing is if there is a race coefficient or a non-Black and a Black eGFR, then obviously the correct recommended estimated GFR is not being reported.

The specific differences for individual patients and for the clinicians who care for them will be relatively small and probably often not that clinically significant for an individual patient, but I think that needs to be reviewed between the patient and the clinician. In general, people who self-identify

as Black will have lower estimated GFRs compared to the way we used to estimate them with a race coefficient and people who are non-Black will have higher estimated GFRs compared to the previous rate. Sometimes those changes, although they may be small, can cross clinical thresholds for things like nephrology consultation or access to kidney transplant or access to certain medications or the diagnosis of CKD. And in that case, it may be one of the reasons to do more tests, such as the cystatin C that Christina mentioned earlier. With that, I'll ask Dr. Pierre if she has anything to add.

Christina Pierre: Yeah. No, I think I covered it pretty well and would just like to emphasize the point that Joe made around just reviewing on a very individualized level with patients essentially and not treating eGFR I guess as absolute truth, but rather recognizing that it is an estimate, is something that we talk about a lot throughout the paper and the need for really individualized care when you're using these estimates.

Randye Kaye: All right. Thank you. Now, can you describe how the clinical laboratory can support the clinical providers, like those in nephrology and primary care, to achieve equity in kidney health if that's possible?

Joseph Vassalotti: I think that we want to meet the clinical laboratory where they are, so what is the clinical laboratory currently doing? If you're reporting the estimated GFR with the recommended CKD-EPI creatinine equation, the 2021 equation, and you're also testing cystatin C in-house and offering that test with a rapid turnaround, and you also report urine albumin to creatinine ratio in milligrams per gram, then really, you're covering most of the recommended tests. If you're not doing those things, of course we want to help you implement the recommended testing.

One next step that laboratories can take to help clinicians order the recommended tests for kidney disease is that we have a CGA Classification of kidney disease, a Cause GFR albuminuria classification, and to help clinicians or facilitate ordering of urine albumin to creatinine ratio, something called the kidney profile can be offered that includes both the estimated GFR and the urine albumin to creatinine ratio with one click of the mouse or one check if it's on a written laboratory report. That test can be combined with other common panels like the basic metabolic panel and the comprehensive metabolic panel.

I think in addition to those things, the clinical laboratory can start to work with the clinicians and the health equity experts, and primary care, and nephrology to evaluate population health and quality improvement. Laboratory values are basically how kidney disease is detected and risk stratified, and accordingly, we can evaluate the vulnerable populations

with the social determinants of health, or the Social Deprivation Index, or other indices of social determinants of health, and to ensure that those populations are receiving the care that they need and deserve. And then they can also work with the clinical communities to decide what kind of quality improvement is necessary, like perhaps improving nephrology consultation or improving blood pressure control or diabetes control. So, I think the laboratory, I think in some settings, it's been called Laboratory 2.0, get the laboratory to outside of the lab and to interact with the clinicians and to impact the patients in the communities that they serve, and that they improve detection, risk stratification, and get into really improving care.

Randye Kaye: So my final question, what are some of the guidance document's key takeaways that you might like to highlight for the readers?

Christina Pierre: I think that the most overarching and far-reaching, I think theme, that's discussed in the guidance document is the fact that race is not a biological classifier. And I think as clinicians and scientists, we're trained to look at genetics and we're trained to look at symptoms and clinical features, but we're not as trained to look necessarily at the social determinants of health and we're not as trained to look at environmental stresses. And so hopefully those guidance document sort of highlights the fact that we need to actually start looking outside of what we're classically trained in to try to explain some of the racial differences in health that we observe.

I also think that, more pertinent to eGFR in and of itself, we do have a growing transgender community and we have a very gender diverse community, and we discussed estimation of kidney function in this community due to intersectionality, right? So, how non-binary gender identities can combine with racialized minority identities to impact kidney health. I think we need to really start thinking about us providers, how we're going to manage these patients. So, which sex coefficient, for example, are we going to use the compute eGFR? Then as it pertains to, again, to kidney disease, early diagnosis and detection is key, largely because chronic kidney disease is silent and often diagnosed in its late stages.

So, I think we as a clinical lab really need to be cognizant of how we measure and report kidney disease biomarkers, as well as standardize our reporting to help support our nephrology and primary care colleagues. And then lastly, just thinking about eGFR as an estimate with multiple sources of error and thinking about interpreting eGFR in the context of each patient essentially, rather than treating it as a source of absolute truth, I think is another important takeaway of the guidance document. Dr. Vassalotti, did you want to add anything?

Joseph Vassalotti: I think we really hit many of the highlights in the previous questions and I think you really summarized a lot of it really nicely. I would just add that this AACC/National Kidney Foundation Guidance Document really builds on the work of the Task Force of the National Kidney Foundation and American Society of Nephrology that recommended the race-free estimated GFR reporting, and also builds on the National Kidney Foundation's Laboratory Working Group's paper that was published in *Clinical Chemistry* in 2022 about implementation for laboratories. I think Christina really touched on a lot of the issues that are new in this document.

I would just add that there is more on cystatin C here, more details on cystatin C in terms of some of the non-GFR determinants for cystatin C, and also for creatinine, to help inform clinicians and laboratorians when one test or the other might be preferable, emphasis on using both biomarkers when precision is required in the absence of the non-GFR determinants; that's nicely covered in Table 3 in the paper. There's also some evidence on urine albumin to creatinine ratio as the missing test and there may be some disparities there, lack of testing there, and there's a table that reviews the approximations of urine albumin-creatinine ratio with urine protein to creatinine ratio, and also urine dipstick for protein, which tests for albumin, which is confusing to clinician sometimes.

And I would point out that urine albumin to creatinine ratio will be standardized, or is on track to be standardized, for 2025. So I think that's an important test for laboratories to emphasize in addition to estimated GFR. And I think we look forward to working with the AACC in the future and laboratorians to implement these tests and the reporting and to improve population-level health. And the last thing I'll say is the National Kidney Foundation is working with the American Society of Nephrology to remove race and ethnicity from the Kidney Donor Risk Index that's used to evaluate deceased donor kidneys with the OPTN and their Minority Affairs Committee. And also, the National Kidney Foundation has a pharmacy engagement program or initiative that's addressing drug dosing and estimated GFR and patient safety that the issues that we've discussed today impact.

Lastly, I think it's a great opportunity for clinicians and laboratories to work together for population health and for health equity. So I'm excited about this and I'm really pleased that we've had this opportunity to collaborate and look forward to additional collaborations.

Randye Kaye: That was Drs. Christina Pierre and Joseph Vassalotti describing the *JALM* Special Report "AACC/NKF Guidance Document on Improving Equity in Chronic Kidney Disease

Care." Thanks for tuning in to this episode of *JALM* Talk, see you next time and don't forget to submit something for us to talk about.